## REMARKS

Claims 1-26 were pending in the present application, claims 1, 9-12, and 21-26 were under examination, and claims 2-8 and 13-20 stood withdrawn. In this paper, claims 9, 10, 12, 21, and 25 are amended and claims 2-8, 11, and 13-20 are cancelled without prejudice to Applicants' right to pursue the cancelled subject matter in one or more related divisional, continuation, and/or continuation-in-part applications. Thus, following entry of the present amendment, claims 1, 9, 10, 12, and 21-26 are pending and under consideration.

### I. THE AMENDMENTS TO THE CLAIMS

The present paper presents an amendment to claims 9, 10, 12, 21, and 25. The amendments to the claims are fully supported by the application as filed and therefore introduce no new matter.

In particular, support for the amendments to claims 9, 10 and 25 may be found, for example, in claim 11 as filed. Support for the amendments to claims 12 and 21 may be found, for example, in claims 12 and 21 as filed.

As the amendments to the claims are fully supported by the application as filed, these amendments introduce no new matter. Entry of the amendments to the claims is therefore respectfully requested under 37 C.F.R. § 1.111.

### II. THE REJECTION OF CLAIMS 10 AND 25 FOR LACK OF ENABLEMENT SHOULD BE WITHDRAWN

Claims 10 and 25 stand rejected for lack of enablement under 35 U.S.C. § 112, first paragraph, as the application allegedly does not enable the skilled artisan to determine the disease status of a patient suffering a disease characterized by aberrant expression of VEGFR2 by measuring VEGFR2 homodimers. In particular, the PTO argues that neither the art nor the instant application as filed describes any correlation between the presence of VEGFR2 homodimers and the status of any disease.

Without acquiescing to the propriety of the rejection, Applicants believe the rejection is moot in view of the amendments to claims 10 and 25. Claims 10 and 25 now recite that the disease status which is determined is either cancer or a disease characterized by aberrant angiogenesis. As the role of activated VEGFR2 in angiogenesis and cancer is well known

(*see*, for example, Wedge *et al.*, 2005, *Cancer Res.* 65:4389-4400 and Rahimi, 2006, *Exp. Eye Res.* 83:1005-1016, attached hereto as Exhibits A and B, respectively) any experimentation required to practice the invention as presently claimed would be routine, rather than undue. Accordingly, Applicants respectfully submit that the rejection of claims 10 and 15 for lack of enablement under 35 U.S.C. § 112, first paragraph is moot and respectfully request its withdrawal.

## III. THE REJECTION OF CLAIMS 12 AND 21-26 FOR LACK OF WRITTEN DESCRIPTION SHOULD BE WITHDRAWN

Claims 12 and 21-26 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking written description in the instant application as filed. In particular, the PTO contends that the application as filed discloses an insufficient number of species of a "binding compound" to support a claim reciting this term. To support this argument, the PTO contends that the present application discloses only one species of binding compound, an antibody. While the PTO concedes that the present application discloses other examples of compounds that can be used as binding compounds, the PTO argues that there are insufficient structural features common to those compounds to satisfy the written description requirement. Applicants respectfully traverse.

Applicants disclose numerous examples of binding compounds, including "an antibody binding composition, an antibody, a peptide, a peptide or non-peptide ligand for a cell surface receptor, a protein, an oligonucleotide, an oligonucleotide analog, such as a peptide nucleic acid, [or] a lectin." *See* the specification at page 30, lines 32-35. Applicants further state that a binding compound can be any "molecular entity capable of specific binding or stable complex formation with an analyte of interest." *See id* at page 30, lines 35-36. Thus, Applicants provide several examples of compounds having known and defined structural features, together with the functional characteristic of a binding compound.

According to the Federal Circuit's decision in *Enzo Biochem., Inc. v. Gen-Probe Inc.*, 63 USPQ2d 1609 (Fed. Cir. 2002), ("*Enzo*"), a genus can be supported by species defined by functional characteristics so long as a correlation between structure and the functional characteristic is known or disclosed. Applicants respectfully submit that such a correlation is known to the skilled artisan.

In the context of claims 12 and 21-26, the binding compounds specifically bind to VEGF receptor complexes. Thus, any of the enumerated compounds that binds to VEGF receptor complexes can be used as a binding compound. In addition to antibodies, and fragments thereof, that bind VEGF receptor complexes, VEGF receptor ligands could also be used as a binding composition. Prior to the filing of the instant application, at least four different isoforms of VEGF were known to the skilled artisan. *See, e.g.*, Tischer *et al.*, 1991, *J. Biol. Chem.* 266: 11947-11954 and Poltorak *et al.*, 1997, *J. Biol. Chem.* 272: 7151-7158, attached hereto as Exhibits C and D, respectively. Thus, the structures of species of binding compounds other than antibodies that have the desired functional characteristic are known to the skilled artisan.

In addition, the instant application teaches that lectins can be used as suitable binding compounds, as set forth above. Applicants respectfully invite the PTO's attention to Vaisman *et al.*, 1997, *J. Biol. Chem.* 265:19461-6, attached hereto as Exhibit E. Vaisman *et al.* indicate that the high affinity receptors for VEGF are heavily glycosylated, and that four different lectins bind these glycosyl residues. *See* Vaisman *et al.* at page 19464, col. 2, paragraph 1. Thus, these lectins constitute at least four additional species within the scope of the term "binding compound" with structures known to the skilled artisan. Applicants respectfully submit that these additional species with known structures having the desired functional characteristic support the entire scope of the term "binding compound" and thus respectfully request that this aspect of the rejection be withdrawn.

The PTO further argues that the specification does not describe a representative number of species within the genus "cleavage-inducing moiety." In particular, the PTO argues that the instant application discloses only a single example of a cleavage-inducing moiety, a photosensitizer.

Applicants respectfully invite the PTO's attention to the specification at page 37, lines 1-12. Here, Applicants disclose at least three specific cleavage-inducing moieties that are sensitizers (*e.g.*, a compound that can be induced to generate a reactive intermediate such as singlet oxygen), 1,4-biscarboxyethyl-1,4-naphthalene endoperoxide, 9,10-diphenylanthracene-9,10-endoperoxide and 5,6,11,12-tetraphenyl naphthalene 5,12-endoperoxide. In addition, Applicants list three references that disclose additional sensitizers suitable for use in the present invention, Di Mascio *et al.*, 1994, *FEBS Lett.* 355:287; Kanofsky, 1983, *J. Biol. Chem.* 258: 5991-5993; and Pierlot *et al.*, 2000, *Meth. Enzymol.*

319:3-20 (attached hereto as Exhibits F, G, and H, respectively. These references disclose at least 10 additional species of sensitizer suitable for use as a cleavage-inducing moiety in the claimed methods. Accordingly, Applicants respectfully submit that the instant application describes several species of cleavage-inducing moieties other than photosensitizers. Therefore, Applicants respectfully request withdrawal of this aspect of the rejection of claims 12 and 21-26 for alleged lack of written description under 35 U.S.C. § 112, first paragraph.

## IV. THE REJECTION OF CLAIMS 1, 9, AND 11 AS ANTICIPATED SHOULD BE WITHDRAWN

Claims 1, 9, and 11 stand rejected as anticipated under 35 U.S.C. § 102(e) by U.S. Patent No. 6,635,421 (the '421 patent). In particular, the PTO asserts that the '421 patent discloses a method for determining the prognosis of prostate cancer that comprises, *inter alia*, measuring VEGF receptor amounts on a tumor sample from a patient and correlating such VEGF receptor amounts with an indication of unfavorable prognosis. Applicants respectfully traverse.

Claim 1 and dependent claims 9 and 11 recite methods for determining disease status that comprise, *inter alia*, measuring amounts of one or more cell surface receptor complexes. As defined in the instant specification, a "complex" refers to "an assemblage or aggregate of molecules in direct or indirect contact with each other." *See* the specification at page 7, lines 28-29. Thus, claim 1 recites a method that comprises measuring amounts of one or more cell surface assemblages or aggregates of molecules.

In contrast, the '421 patent discloses methods that comprise measurement of amounts of VEGF protein or m-RNA. Thus, the '421 patent teaches methods that rely on measurement of amounts of a particular molecule, not aggregates or assemblages of molecules. As such, the '421 patent fails to teach each and every element of the invention defined by claims 1, 9, and 11, and thus cannot anticipate such claims. *See Merck & Co. v. Teva Pharmaceuticals USA, Inc.*, 68 USPQ2d 185 (Fed. Cir. 2003). Accordingly, Applicants respectfully request that the rejection of claims 1, 9, and 11 as anticipated by the '421 patent be withdrawn.

## V. THE REJECTION OF CLAIMS 1, 9, 11, 12, 21-24, AND 26 AS OBVIOUS SHOULD BE WITHDRAWN

Claims 1, 9, 11, 12, 21-24, and 26 stand rejected as obvious over the '421 patent in view of U.S. Patent No. 6,627,400 (the '400 patent). In particular, the PTO contends that it would be obvious to use the methods of the '400 patent for determining populations of surface membrane proteins in the methods of the '421 patent for determining prognosis of prostate cancer that comprise, *inter alia*, measuring amounts of VEGF receptor. Applicants respectfully traverse.

Independent claims 1 and 21 and dependent claims 9, 11, 12, 22-24, and 26, each recite methods for determining a disease status of a patient that recite, *inter alia*, measuring amounts of cell surface receptor complexes. As discussed above, such receptor complexes are defined to be "an assemblage or aggregate of molecules in direct or indirect contact with each other." Neither the '421 patent nor the '400 patent, either alone or in combination, teach or suggest a method for determining the disease status of a patient that comprises measuring an amount of "an assemblage or aggregate of molecules in direct or indirect contact with each other." As such, the '421 patent and '400 patent, either alone or in combination, fail to teach or suggest each and every element of the invention as presently claimed. As the combination of cited references fails to teach each and every element of the invention as claimed, Applicants respectfully submit that the claims are not obvious over the cited references. *See In re Gartside*, 53 USPQ2d 1769 (Fed. Cir. 2000).

Further, nothing in either the '421 patent or the '400 patent provides any motivation to modify the teachings of these documents to obtain the claimed invention. For example, no teaching of the '421 patent suggests that amounts of receptor complexes, rather than amounts of VEGF receptor protein or mRNA, should be measured in the methods of the '421 patent. Absent such motivation to modify the cited references, the PTO cannot establish *prima facie* obviousness of the claimed invention. *See In re Kotzab*, 55 USPQ2d 1316 (Fed. Cir. 2000). As such, for this additional reason, the rejection of claims 1, 9, 11, 12, 21-24, and 26 as obvious over the '421 patent in view of the '400 patent should be withdrawn.

Finally, Applicants note for the record that Applicants do not admit that the '400 patent is prior art to the present application.

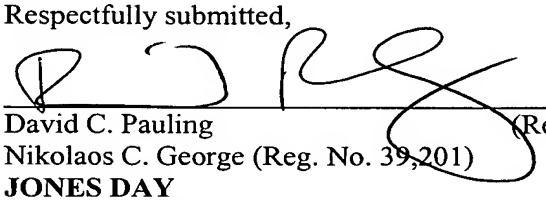
## VI. CONCLUSION

In view of the foregoing, Applicants respectfully submit that the present application is in condition for allowance and earnestly request an early indication of the same.

No fee is believed due with this response other than the fee for the extension of time for response. However, should the Commissioner determine otherwise, the Commissioner is hereby authorized to charge any required fee(s) to Jones Day Deposit Account No. 50-3013 (Order No. 949677-999131). A copy of this sheet is enclosed for such purpose.

Respectfully submitted,

Date: January 5, 2007



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